left in place, we believe the relatively short observation period was sufficient. We also believe from this study that the location of pulmonary vessels (which are the vessels heard by the Doppler catheter) are difficult to predict without using the Doppler catheter. There was little predictability of vessel location in these segmental and subsegmental airways, making use of this device vital in avoiding contact with major vessels lying adjacent to the airway walls. As far as the question of creating the passages in segmental or subsegmental bronchi is concerned, we believe this has little relevance because both segmental and subsegmental bronchi are equally surrounded by emphysematous lung tissue, as can be seen on high-resolution computed tomographic scans. Manipulation of the of the catheters was easy in the lower lobes, whereas in the upper lobes the procedure required some training because of the unfavorable angle of the bronchoscope and the need to withdraw the Doppler catheter and introduce the cautery probe while keeping the tip of the bronchoscope stationary. All considerations about the clinical effects of the airway bypass procedure are beyond the purpose of this study; namely the effect of secretions in the patency of the passages, the best way to keep the passages steadily open, and the clinical benefit of the procedure.

Our study proved that the airway bypass procedure is safely feasible in normal human subjects, as well as in patients with emphysema requiring lung transplantation. The Doppler device used to detect pulmonary vessels is effective, and the cautery probe enables safe creation of airway bypasses. These clinical results support further investigation of the efficacy of the airway bypass procedure in patients with emphysema. In particular, animal studies with long-term follow-up are ongoing to develop the ideal stent to keep the passages open.

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Discussion

Dr Scott J. Swanson *(New York, NY).* This well-presented article discusses a novel concept first presented at this year's meeting of The Society of Thoracic Surgeons by Dr Lausberg of Dr Cooper's group that examines the feasibility of creating small passages from segmental or subsegmental airways into the parenchyma of the lung as a treatment for emphysema using a Doppler device for guidance and a radiofrequency catheter to create the passage. The idea is to provide nonanatomic routes into the lung to permit improved ventilation. At the prior presentation, this method was used ex vivo in human patients with emphysema undergoing transplantation and was shown to improve a surrogate forced expiratory volume in 1 second calculation by 78%. Today's article is an extension of that study and was performed in vivo at the time of either lobectomy for lung cancer or bilateral lung transplantation for emphysema. From 1 to 5 passages were created per patient. In the 10 patients undergoing lobectomy, there was a 20% incidence of mild bleeding, and in the 5 patients undergoing transplantation, this was not observed. The conclusion by the authors is that this procedure is safely feasible.

I would like to make 1 comment and ask 4 questions. It is a privilege to discuss an article by such a renowned group that has made many seminal contributions in advancing the treatment of patients with emphysema.

First, did the pathologists examine the lung specimens, and, if so, what did they see at the site of the neopassages? Was there hemorrhage, and how big were the channels?

Second, it is widely known and my colleagues from Boston have shown that obstruction to air flow in emphysema occurs in the very distal airways. How many of the passages in this experiment were in the segmental airways and how many were in the subsegmental airways, and why do you surmise that this might have an effect on the trapped ventilation that occurs much more distally?

Third, is it true to conclude that this is safe and feasible when the observation period after the procedure was minutes rather than hours or days? Are there plans to carry this out in an animal model to truly show safety before attempting this in human subjects?

Fourth, if stenting the passages is the plan to keep the channels patent, we know that stenting larger airways and the esophagus for benign lesions is fraught with problems from the radial traction and occlusion from secretions. How will these issues be addressed?

Dr Rendina. At the beginning of your discussion, you mentioned a 20% rate of bleeding considering the 2 episodes occurring in the 10 patients undergoing lobectomy. The denominator should, however, be considered the 47 passages created overall and not the 10 patients undergoing lobectomy, so that this rate drops to 4.2%. Regarding pathology, we had performed accurate pathologic studies in previous animal experiments, including more than 100 transbronchial passages, and we could demonstrate that the passages were about 1.5 mm in diameter, there was no bleeding around the site of the passage, and there was no necrosis of the

surrounding tissues. Therefore, we did not find it necessary to repeat pathologic examinations in this study.

Your second question refers to the pathophysiology at the basis of our work. The present study is focused only on safety and feasibility, but I will try to address the question of peripheral airway obstruction. The concept is that unless marked intrinsic small airway disease is present, the obstruction of the peripheral airways is due to the hyperinflation of the lung, and it presents mostly on expiration. Within the hyperinflated lung, collateral ventilation allows the movement of gas independently from the anatomic airways. The passages created should bypass this obstruction on expiration, while leaving inspiration unmodified. The question of creating the passages in segmental or subsegmental bronchi has little relevance because both segmental and subsegmental bronchi are equally surrounded by emphysematous lung tissue, as can be seen on high-resolution computed tomographic scans.

Concerning safety, the crucial point of this study was to demonstrate in human subjects what we had already performed in animal studies; that is, that the detection of the vessels around the bronchus was accurate and that transbronchial holes reaching into the lung parenchyma could be safely made. Therefore, we considered that a short observation time was sufficient.

As far as stents are concerned, my answer can be only speculative because stents were not used in this study. It might, however, be that the presence of a foreign body might entail further risk. I also concur with you that the secretions potentially occluding the stent can be a problem. However, one has to consider that secretions are produced by the bronchi and not by lung parenchyma. Therefore, in principle, secretions should not affect the patency of the stents when we use them in the future.

Dr Walter Klepetko *(Vienna, Austria).* I would like to ask 2 questions. First, were those patients who underwent lobectomy emphysematous patients?

The other question is directed to the ventilation patterns measured on the respirator. I am sure you have measured them before and after the procedure, and at least in the patients with end-stage emphysema with the indication for transplantation, there must have been an immediate and dramatic change. Can you give us some results about that?

Dr Rendina. The patients undergoing lobectomy were not severely emphysematous, with the exception of one patient. We have the preoperative spirometric data, but the postoperative spirometric data are irrelevant because the lobe in which the bypasses were done was removed. Also, the purpose of this study was not to demonstrate benefit. Patients undergoing transplantation, on the contrary, were obviously severely emphysematous. In one such patient, the free collapse was measured, and it was found to be improved; however, that was done in only one patient.

Dr Klepetko. In the transplantations, have you observed an immediate increase of the ventilation parameters? If you have such a dramatic improvement as you have been demonstrating in the experimental setting, you must have an immediate effect on the table there and you should measure that.

Dr Rendina. Yes, I answered that. This was not the purpose of this study, but free collapse in the last patient demonstrated improvement.

Dr Carlos Saldarriaga *(Medellin, Colombia).* Do you think this technique is feasible for endoscopic treatment of bullous emphysema?

Dr Rendina. The purpose of this procedure at the present time is not the treatment of bullae. The concept at the basis of this study is collateral ventilation and the ability to create exit pathways that are alternative to airways collapsed during expiration by the hyperinflated lung compressing from the outside.

Dr Jean Deslauriers *(Sainte-Foy, Quebec, Canada).* Erino, I have to congratulate you. I think you and Joel are kind of an ideal team.

I have a couple of worries about this procedure. First, concerning these stents, you have not shown the safety of the procedure. Many patients with emphysema have pulmonary hypertension to begin with. When you insert the stents, if you were to hit a vessel, it would be instant death. If you were to do a pneumothorax, it would also be instant death because these patients have no reserve.

Second, if you leave the stents in place for some days, in the patient with true emphysema who has a lot of purulent secretions and is receiving cortisone, you have inserted a foreign body. The lung moves up and down and the pulmonary artery that beats. I think you have exactly the right conditions for a catastrophic erosion that might occur within a week or 2 or 3 weeks. I would be really worried about putting in foreign bodies. Obviously the stents are going to be bigger as time goes on, so that they do not get obstructed. You said the secretions would not go in the stents, but they will because these patients are infected. They will cough. Some of this pus is going to go right outside the bronchi. These are perfect conditions for abscesses and erosions.

My second comment has to do with Dr Swanson. You are dealing with a disease that affects the periphery of the lung. It is common knowledge that emphysema is basically in the periphery of the lung and not in the center of the lung, yet you are putting these stents right where the lung is the most normal. How do you expect to treat a disease that is basically on the surface by putting these stents in the middle of the lung?

Other than that, I think the article is wonderful, and I recognize Joel's innovative ideas in the field of emphysema and his crusade to solve the problem, but I am really worried about these stents.

Dr Rendina. Thank you, Dr Deslauriers, for your comments and questions. Most of the points that you make, however, concern issues that have not been addressed in this study. I wish to remind you that stents were not used, and no follow-up beyond surgical intervention was required in this study. Nevertheless, your comments are pertinent and important with regard to the overall procedure. We share your concern about the potential danger of stents, particularly in the face of pulmonary hypertension. We have not observed problems related to the various stents that we have used in our animal experiments, although we are still in the process of developing the ideal stent. In addition, we tend to consider pulmonary hypertension as an exclusion criterion in our forthcoming clinical studies.

The occurrence of pneumothorax was also a matter of concern. We have therefore filled the chest with saline solution after creating the holes in the bronchi, and we have noticed no air leaks from the parenchyma. Therefore, this study confirmed that pneumothorax should not be expected as a complication.

The issue of secretions occluding the passage cannot be solved until the procedure undergoes clinical experimentation. There are patients with emphysema who have many secretions and others who do not or have much less. Although we tend to believe that secretions will not affect the patency of the passages, our intention is to exclude patients with extensive secretions from future clinical trials.

Last, you argue that the most destroyed areas are located at the periphery of the lung, and yet we create the passages through the bronchi in the most central part of the lung, which presumably is healthier. It is questionable whether in severe homogenous emphysema the healthier tissue is that surrounding the airway. In addition, the anatomic basis of collateral ventilation resides in the fact that air can move freely within the lung parenchyma, and therefore one passage created in a given segmental or subsegmental bronchus can, in theory, drain the whole lobe. Air-dried lung preparations confirm what can be clearly seen on any high-resolution computed tomographic scan of emphysematous lungs. The patterns of parenchymal destruction reach deep into the lung and around the airways, and in our study we could actually see destroyed lung through the passages in those patients who had emphysema.